

Substitute for form 1449A/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

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Sheet 1 of 5

Complete if Known

Application Number	10/579,160
Filing Date	March 1, 2007
First Named Inventor	Mary Ellen Rybak
Art Unit	1623
Examiner Name	Lewis, Patrick T.
Attorney Docket Number	13566.105023

U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. ¹	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code ² (if known)			
		US 20040108086	06-10-2004	Takahashi et al.	
		US 20040002602	01-01-2004	Francesch et al.	
		US 5,908,835	06-01-1999	Bissery	
		US 7,241,892	07-10-2007	Cuevas et al.	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
		Country Code ³ - Number ⁴ - Kind Code ⁵ (if known)				
		WO 00/69862	11-23-2000	Pharma Mar S.A.		
		WO 01/87894	11-22-2001	Pharma Mar S.A.		

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NON PATENT LITERATURE DOCUMENTS

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		Bernacki et al., "In Vitro Antitumor Activity of 9-Nitro-Camptothecin as a Single Agent and in Combination with other Antitumor Drugs" Annals of the New York Academy of Sciences, vol. 922 (1), p. 293, December 2000	
		Burstein et al., "Phase I study of Doxil and Vinorelbine in Metastatic Breast Cancer," Annals of Oncology, vol. 10, pages 1113-1116, 1999, XP8086751	
		Delaloge et al., "Ecteinascidin (ET-743) in heavily pretreated refractory sarcomas: Preliminary evidence of activity," Eur. J. Cancer, vol. 35, suppl. 4, page S271, Abstract No. 1080, Sept 15, 1999	
		D'Incalci et al., "Mode of action of Ecteinascidin-743 (ET-743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, pages 3872s-3873s, Abstract of Plenary Session 7, November 16-19, 1999	
		European Medicines Agency (EMA), "Scientific Discussion" from the European Public Assessment Report for Yondelis®, Revision 1, published March 31, 2008, downloaded from the internet on April 2, 2008, from the website << http://www.emea.europa.eu/humandocs/Humans/EPAR/yondelis/yondelis.htm >>	
		Garcia-Carbonero et al., "Population pharmacokinetics of ecteinascidin 743 in patients with advanced soft tissue sarcoma," Clinical Cancer Research, vol. 6, Supplement, Abstract 211, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Giovanna et al., "Importance of DNA repair mechanisms for the sensitivity of tumor cells to ET-743," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 303, November 16-19, 1999	
		Hoekman et al., "A phase I/II study of dose-escalated docetaxel given two weekly in combination with a fixed dose of G-CSF," European Journal of Cancer, vol. 37, page S76, Abstract 270, October 22, 2001	
		Hornicek et al., "In vitro effect of the tetrahydroisoquinoline alkaloid Ecteinascidin-743 (ET-743) on chondrosarcoma (CHSA) cells," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 304, November 16-19, 1999	

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		Jimeno et al., "Pharmacokinetics (PK)/Pharmacodynamic (PD) Relationships in Patients (PT) Treated With Ecteinascidin-743 (ET-743) Given As 24 Hours Continuous Infusion (CI)," Journal of Clinical Oncology, ASCO Annual Meeting Proceedings, Abstract No. 744, May 15-18, 1999	
		Jin et al., "The antitumor agent Ecteinascidin 743 (ET743), inhibits transcriptional activation of the MDR1 Gene by multiple inducers," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 302, November 16-19, 1999	
		Lopez-Lazaro et al., "Exploratory evaluation of the potential predictors for dose-limiting toxicities (DLTs) in patients treated with Ecteinascidin-743 (ET-743) as a 24-h intravenous (iv) infusion every 3 weeks and its relationship to pharmacokinetics (PK)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 308, November 16-19, 1999	
		Lyass et al., "Phase I Study of Doxil-Cisplatin Combination Chemotherapy in Patients with Advanced Malignancies," Clinical Cancer Research, vol. 7, pages 3040-3046, October 2001, XP8086753	
		Michaelson et al., "A Phase I Study of 9-Nitrocamptothecin Given Concurrently with Capecitabine in Patients with Refractory, Metastatic Solid Tumors," Cancer, vol. 97 (1), pages 148-154, January 1, 2003	
		Rosing et al., "Pharmacokinetics (PK) of Ecteinascidin-743 (ET-743) in three different phase I trials," Proceedings of the American Association for Cancer Research, vol. 40, pp 81, abstract no. 542, March 1999	
		Ryan, D.P. "Studies with Ecteinascidin-743 (ET-743) A Marine Alkaloid," Cancer Invest, vol. 18 (suppl 1), pp 112, abstract no. 87, January 2000, from the Chemotherapy Foundation Symposium XVII Innovative Cancer Therapy for Tomorrow, November 3-6, 1999, New York, NY	
		Scotto et al., "Ecteinascidin 743, a novel chemotherapeutic agent that targets transcriptional activation of a subset of genes, including MDR1," Clinical Cancer Research, vol. 6, Supplement, Abstract 210, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Shertzer et al., "Protection Against Carbon Tetrachloride Hepatotoxicity by Pretreatment with indole-3-carbinol," Exptl. Molec. Pathol., vol. 46, pp. 180-189 (1987)	
		Shertzer et al., "Protection from N-Nitrosodimethylamine Mediated Liver Damage by Indole-3-carbinol," Exptl. Molec. Pathol., vol. 47, pp. 211-218 (1987)	

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		Taamma et al., "Ecteinascidin-743 (ET-743) 24 hour continuous intravenous infusion (CI) phase I study in solid tumors (ST) patients (pts)." Proceedings of the American Association for Cancer Research, vol. 39, pp 323, abstract no. 2207, March 1998	
		Taamma et al., "Ecteinascidin-743 (ET-743) in heavily pretreated refractory sarcomas: early results of the French experience," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3791s, Abstract 309, November 16-19, 1999	
		Takebayashi et al., "Multidrug Resistance Induced by DNA Minor Groove Alkylation of Ecteinascidin 743 (Et743)," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3851s, Abstract 602, November 16-19, 1999	
		Takebayashi et al., "Nucleotide excision repair-dependent cytotoxicity of Ecteinascidin 743," Clinical Cancer Research, vol. 6, Supplement, Abstract 207, page 4508s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	
		Ten Hagen et al., "Pegylated Liposomal Tumor Necrosis Factor-Alpha Results in Reduced Toxicity and Synergistic Antitumor Activity after Systemic Administration in Combination with Liposomal Doxorubicin (Doxil) in soft tissue Sarcoma-Bearing Rats," Int. J. Cancer, vol. 97, pages 115-120, 2002	
		Twelves et al., "Phase I Trials with ET-743, a marine derived (MD) anticancer agent," Eur. J. Cancer, vol. 35, suppl. 4, page S283, Abstract No. 1135, Sept 15, 1999	
		Twelves et al., "Phase I and pharmacokinetic study of Yondelis TM (Ecteinascidin-743; ET-743) administered as an infusion over 1 h or 3 h every 21 days in patients with solid tumours," European Journal of Cancer, vol. 39, p. 1842-1851, 2003; available online August 14, 2003	
		van Kesteren et al. "Clinical Pharmacology of the Novel Marine-derived Anticancer Agent Ecteinascidin 743 Administered as a 1- and 3-h Infusion in a Phase I Study," Anti-Cancer Drugs, Vol. 13, No.4, pgs. 381-393, April 2002	
		Weiwei et al., "Potent antitumor activity of ET-743 against human soft tissue sarcoma cell lines," Proceedings of the 1999 AACR-NCI-EORTC International Conference, Clinical Cancer Research, volume 5, Supplement, page 3790s, Abstract 305, November 16-19, 1999	

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		Zelek et al., "Preliminary results of phase II study of ecteinascidin (ET-743) with the 24 hour (H) continuous infusion (CI) q3week schedule in pretreated" Clinical Cancer Research, vol. 6, Supplement, Abstract 212, pages 4508s-4509s, NCI-EORTC-AACR Symposium On New Drugs In Cancer Therapy, November 7-10, 2000	

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